

10001

FITZPATRICK, CELLA, HARPER & SCINTO

1900 K STREET, N.W.
WASHINGTON, D.C. 20006-1110
(202) 530-1010

Facsimile:(202) 530-1055
FACSIMILE COVER SHEET

FAX RECEIVED

APR 06 2003

GROUP 1600#15
B.93
4/14/03

TO: Examiner Christopher Nichols, Ph.D.
Group Art Unit 1647
USPTO

OFFICIAL

FROM: Haiyan Chen
202-721-5492 (direct dial)

RE: Application No. 09/674,913
Attorney Docket No. 01702.401600

FAX NO.: 703-872-9305

DATE: April 2, 2003

NO. OF PAGES: 11
(including cover page)

TIME:

SENT BY: K.S. Poulton

MESSAGE

Please see the attached.

**IF YOU DO NOT RECEIVE ALL THE PAGES
PLEASE CALL 202-530-1010 AS SOON AS POSSIBLE.**

Note: We are transmitting from a Canon Model FAX-L770
(compatible with any Group I, Group II or Group III machine).

THIS FACSIMILE MESSAGE AND ACCOMPANYING DOCUMENTS ARE INTENDED ONLY FOR THE USE OF THE ADDRESSEE INDICATED ABOVE. INFORMATION THAT IS PRIVILEGED OR OTHERWISE CONFIDENTIAL MAY BE CONTAINED THEREIN. IF YOU ARE NOT THE INTENDED RECIPIENT, YOU ARE HEREBY NOTIFIED THAT ANY DISSEMINATION, REVIEW OR USE OF THIS MESSAGE, DOCUMENTS OR INFORMATION CONTAINED THEREIN IS STRICTLY PROHIBITED. IF YOU HAVE RECEIVED THIS MESSAGE IN ERROR, PLEASE NOTIFY US IMMEDIATELY BY TELEPHONE OR FACSIMILE AND MAIL THE ORIGINAL TO US AT THE ABOVE ADDRESS. THANK YOU.

HC/ksp

DC_MAIN 128617 v 1

01702.401600

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | |
|---|---|--------------------------------------|
| In re Application of: |) | |
| GUSTAV GAUDERNACK, ET AL. |) | Examiner: Christopher Nichols, Ph.D. |
| Application No.: 09/674,913 |) | Group Art Unit: 1647 |
| Filing Date: May 25, 2001 |) | |
| Int'l Appl. No.: PCT/NO99/00141 |) | |
| Int'l Appl. Filing Date: April 30, 1999 |) | |
| For: FRAMESHIFT MUTANTS OF |) | April 2, 2003 |
| BETA-AMYLOID PRECURSOR |) | |
| PROTEIN AND UBIQUITIN-B |) | |
| AND THEIR USE |) | |

Commissioner for Patents
Washington, D.C. 20231

LETTER ACCOMPANYING RULE 132 DECLARATION (VIA FACSIMILE)

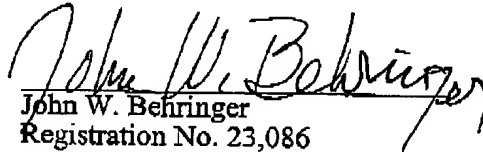
Sir:

Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 of Professor Gustav Gaudernack. The Declaration is submitted to present additional data to show that the claimed invention satisfies the requirements of 35 U.S.C. § 112, first paragraph.

Applicants wish to thank the Examiner for agreeing to conduct an interview with Applicants' representative on April 10 prior to acting on the case.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 530-1010. All correspondence should continue to be directed to our address given below.

Respectfully submitted,


John W. Behringer
Registration No. 23,086
Attorney for Applicants

FITZPATRICK, CELLA, HARPER & SCINTO
30 Rockefeller Plaza
New York, New York 10112-3801
Facsimile: (212) 218-2200

JWB/HC

DC_MAIN 128283 v 1

01702.401600

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | |
|---|---|--------------------------------------|
| In re Application of: |) | |
| | : | Examiner: Christopher Nichols, Ph.D. |
| GUSTAV GAUDERNACK, ET AL. |) | |
| | : | Group Art Unit: 1647 |
| Application No.: 09/674,913 |) | |
| | : | |
| Filing Date: May 25, 2001 |) | |
| | : | |
| Int'l Appl. No.: PCT/NO99/00141 |) | |
| | : | |
| Int'l Appl. Filing Date: April 30, 1999 |) | |
| | : | |
| For: FRAMESHIFT MUTANTS OF |) | |
| BETA-AMYLOID PRECURSOR | : | |
| PROTEIN AND UBIQUITIN-B |) | |
| AND THEIR USE | : | |

DECLARATION UNDER 37 C.F.R. §1.132
OF PROF. GUSTAV GAUDERNACK

I, Gustav Gaudernack, of Sandvika, Norway, do hereby declare as follows:

Background

1. I obtained a Cand.real (Ph.D. equivalent) in 1972 from the University of Oslo in Norway.

2. I am a senior scientist at the Norwegian Radium Hospital, a position I have held since 1995. I am also Chairman of the Section for Immunotherapy at Norwegian Radium Hospital. Attached, as Exhibit A, is a copy of my curriculum vitae.

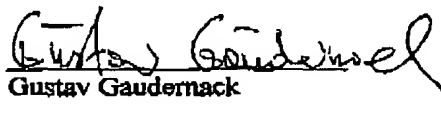
3. I have supervised experimental work to determine whether certain peptide fragments of mutant β -amyloid protein and mutant ubiquitin-B protein found in Alzheimer's disease patients are capable of stimulating the proliferation of Alzheimer-specific cytotoxic T lymphocytes that are useful for killing cells producing mutant β -amyloid and ubiquitin-B proteins. The experiments are briefly described below.

4. Peripheral blood mononuclear cells (PBMC) were isolated from a patient (HUCL120) with a slowly developing form of Alzheimer's disease. The PBMC were washed twice in RPMI 1640 medium (RPMI), suspended in 3 ml RPMI/15% pooled heat inactivated human serum (complete medium), and cultured in 24-well flat bottom plates for 7 days with a cocktail of peptides—Sequence ID Nos. 1, 3, 5, 6 and 10—at a concentration of 12.5 mM each. The cultured cells were then washed, counted and adjusted to 0.5 million cells/ml in complete medium. Fifty thousand cells were seeded in triplicates in 96-well plates. To each well, one of the following was added: 1) 100 microliter complete medium; 2) 100 microliter complete medium containing 50,000 irradiated autologous PBMC, as antigen presenting cells (APC); 3) 100 microliter complete medium containing 50,000 irradiated autologous PBMC and a peptide selected from the group consisting of Sequence ID Nos. 1, 3, 5, 6 and 10, at 25 mM; 4) 100 microliter complete medium containing 50,000 irradiated autologous PBMC and 1 U/ml interleukin 2 (IL-2). Cultures without peptide added were used as a negative control while cultures with IL-2, a major growth factor for T cells, were used as a positive control. ^3H -Thymidine (3.7×10^7 Bq/well) was added to the cultures on day 2. On day 3, cells were harvested on filters and ^3H -Thymidine incorporation was measured using a Packard scintillation counter.

Proliferation was given as mean counts per minute (cpm) of the triplicates. The test results are shown in Figures 1 and 2, attached as Exhibit B.

5. Figure 1 shows that Sequence ID No.1, a peptide fragment of the mutant β -amyloid protein unique to Alzheimer's disease cells, stimulated the proliferation of specific c T cells isolated from an Alzheimer's disease patient. Figure 2 shows that of the five peptides (Sequence ID Nos. 1, 3, 5, 6 and 10), the peptide having Sequence ID No.1 induced the most T cell proliferation. As the T cell response observed is a "recall type" of immune response, these results demonstrate that Sequence ID No.1 is capable of stimulating the proliferation of memory T lymphocytes that are specific for a peptide generated in patients with Alzheimer's disease cells bearing the mutant β -amyloid protein fragment.

6. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed by me to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of any patent that might issue on the above-identified application.


Gustav Gaudernack

02.04.03
Date

Curriculum Vitae

Name: Gustav Gaudernack
born in Sandvika, Norway, December 11, 1943

Position: Chairman, Section for Immunotherapy, Institute of Cancer Research, The Norwegian Radium Hospital, University of Oslo

Education: Cand.real (Ph.D. equivalent) in Biochemistry, University of Oslo, 1972

APPOINTMENTS

- Chairman, Section for Immunotherapy, Institute of Cancer Research, The Norwegian Radium Hospital, University of Oslo, 1995-
- Guest Professor in Immunotherapy, Medical Faculty, University of Bern, Switzerland, 2000-2003.
- Senior Scientist, The Norwegian Cancer Society, Institute of Transplantation Immunology, The National Hospital, University of Oslo 1986-1995.
- Research fellow, The Norwegian Cancer Society, Institute of Transplantation Immunology, The National Hospital, University of Oslo, 1983-1986.
- Research fellow, The Norwegian Cancer Society, University of Tromsø, 1979-1983.
- Research fellow (Arthritis Foundation), University of Minnesota, Minneapolis, USA, 1980-1981.
- Research fellow, Department of Immunology, University of Tromsø, 1973-1979.
- Visiting fellow, Department of Biochemistry, University of Tromsø, 1972.

HONORS

- Medinnovas Idepris (with Tobias Gedde-Dahl d.y.), 1993
- Medical Faculty Institute of Laboratory Medicine. RH, Strategy Prize (with Bjarne Bogen), 1994

ORGANIZATION AND DIRECTORSHIP OF INTERNATIONAL MEETINGS

- Tromsø Summer School in Experimental Medicine and Biology, 1981.
- The annual Winter Meeting of the Norwegian Biochemical Society, 1990.
- 1st Scandinavian Seminar on Cancer Vaccines, The Norwegian Radium Hospital, 1995
- Scandinavian Seminar on Tumor Immunology and Immunotherapy, Oslo, 2000.
- Merck Symposium on GM-CSF as adjuvant in cancer vaccines, Oslo, 2000
- Cellular Immunotherapy, 18th UICC-ICC Congress, Oslo, 2002
- Cancer Immunology and Immunotherapy Summer School, Island of Spresen, 2003
-

EDITORIAL BOARDS

- Journal of Immunotechnology
- Regular referee for Scandinavian Journal of Immunology, Tissue Antigens, Blood and Medical Oncology
- Referee for Nature Cancer Reviews

CLINICAL TRIALS

- Organized and participated in a large number of investigator initiated and industry sponsored clinical trials of tumor vaccines, including two immuno-gene therapy trials. These trials include the first study of a ras peptide vaccine (1993) and the first study of telomerase peptide vaccination in cancer patients (2000).
- Two immuno-gene therapy trials with mRNA transfected dendritic cells and participation in a EORTC trial of recombinant MAGE-3 protein vaccine in melanoma patients.

FIG. 1

Recognition of seq id no 1 by TLC55
from Alzheimer patient HUCL120

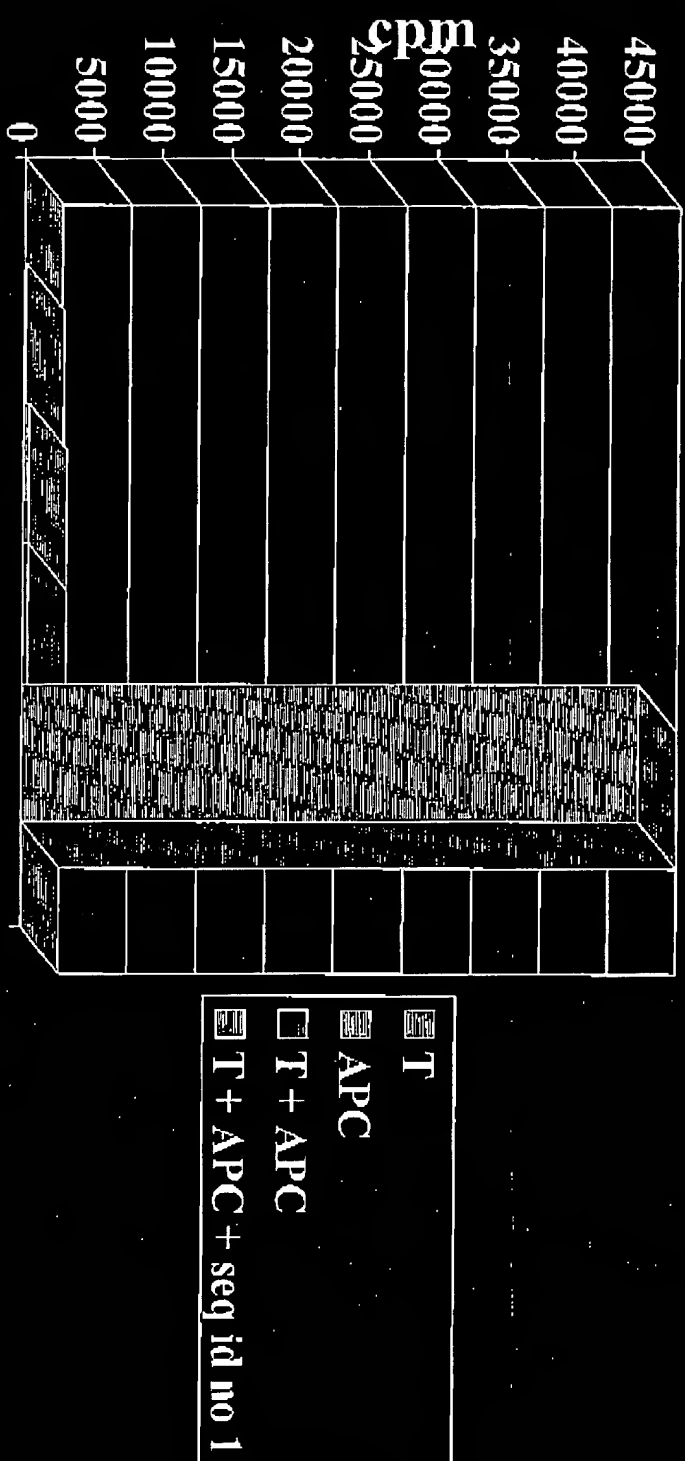


FIG. 2

**T cell responses against frameshift peptide
seq id no 1 in Alzheimer patient HUCLJ 20**

